REMARKS/ARGUMENTS

Former claims 1 to 20 of record have been cancelled in favor of a replacement set of claims 21 to 40 which are believed to better define the scope of protection sought by the Applicant and address all the issues raised in the Examiner's Report of June 30, 2005.

New claims 21 to 31 are directed to a method of treating inflammatory and/or erosive aspects of arthritis in a mammal by administering a proprotein convertase inhibitor, preferably PDX, a derivative of PDX, Dec-RVKR-CH_2Cl or any combination thereof. Support for new claims 21 to 31 may be found in the specification as originally filed. In particular, support for a "proprotein convertase", may be found, for example, at page 9, lines 21 to 24 where it states "...[f]urin-like protease activity includes the activity of proprotein convertases such as PACE4, PC5/6 or PC7". [Emphasis added.] Furthermore, support may be found at page 2, line 26 to page 3, line 3 where classification of proprotein convertases into various subgroups is discussed according to their tissue distribution.

Support for a "derivative of PDX" may be found in the specification, for example, at page 5, line 22 to page 6, line 14. U.S. Patent No. 6,022,855, which is incorporated by reference, teaches reagents, i.e. PDX and its derivatives, for inhibiting furin endoprotease activity. When the specification provides definitions for terms that appear in the claims, then the specification can be used in interpreting the claim language (*See* Phillips v. AWH Corp. (Fed. Cir. Jul. 12, 2005)).

Support for Dec-RVKR-CH_2Cl may be found in the specification, for example, at page 24, line 20 to page 26, line 2.

New claims 32 to 34 are directed to a method of inhibiting synovial cell growth in a mammal by administering a proprotein convertase inhibitor, preferably PDX, or a derivative of PDX. Support for these claims may be found in Example 8 at page 27.

New claims 35 to 40 are directed to a method of blocking proprotein convertase-mediated endoproteolytic activation of a mature form of a protein in a synovial cell by administering a proprotein convertase inhibitor, preferably PDX, a derivative of PDX, Dec-RVKR-CH_2Cl or any

combination thereof. Support for these claims may be found in Examples 3, 4, 5, 7 and 8 at pages 21 to 27.

Election/Restrictions

The Examiner maintains the restriction/election requirement and has finalized her decision regarding the election of the claims of Group I, Group G (i.e. the compound capable of inhibiting a proprotein convertase) and species PDX (of Group G). The Examiner has further upheld the requirement for an election of species of inflammatory diseases for ease of the patentability search.

Former claims 1 to 20 have been cancelled without prejudice or disclaimer in favor of new claims 21 to 40, thus rendering moot the election/restriction requirement thereto. Applicant reserves the right to prosecute the subject matter of the cancelled claims in one or more divisional applications.

In essence, new claims 21 to 40 are directed to methods of treating inflammatory and/or erosive aspects of arthritis. In light of the restriction to a specific class of "inflammatory diseases", and the definition of "proprotein convertase" provided in the description, Applicant respectfully submits that the Examiner's patentability search of the claimed subject matter should not necessitate an election of species PDX.

35 USC §112, 1st Paragraph (Written Description) – Claims 1 to 18

Claims 1 to 18 have been rejected on the basis that the claimed subject matter has not been adequately described in the specification due to the vast number of compounds and diseases covered by the scope of these claims. The basis for the Examiner's rejection is that the single species, "PDX" (and "rheumatoid arthritis"), as described in the application is not sufficient to show possession of the entire genus, "a compound capable of inhibiting a proprotein convertase" (and "inflammatory diseases"). The Examiner therefore concludes that the written description does not support a claim encompassing *all* compounds capable of inhibiting a proprotein convertase for activity in inflammatory diseases based on a written description for the use of PDX for treating rheumatoid arthritis.

Claims 1 to 18 have been cancelled thus rendering moot the rejection thereto. Applicant respectfully submits that new claims 21 to 40 satisfy the written description requirement for treating inflammatory/erosive aspects of arthritis using a proprotein protease inhibitor.

Support for a "proprotein convertase", may be found, for example, at page 9, lines 21 to 24, where it states "...[f]urin-like protease activity includes the activity of proprotein convertases such as PACE4, PC5/6 or PC7." [Emphasis added.] Moreover, support for a "derivative of PDX", may be found in the specification, for example, at page 5, line 22 to page 6, line 14. U.S. Patent No. 6,022,855, incorporated by reference, teaches reagents, i.e. PDX and its derivatives, for inhibiting furin endoprotease activity.

Support for preferred "proprotein convertase inhibitors", may be found, for example, in Example 6 at pages 23 to 26 which discloses administration of PDC and Dec-RVKR-CH_2Cl, the latter being a synthetic peptide that mimics the proprotein recognition site. Further, at page 24, lines 20 to 27, it states "...[s]uch inhibitor has been shown to efficiently inhibit the enzymatic activity of most members of the proprotein convertases including furin, PC6B, PC3, PC2, PACE-4 and PC7".

35 USC §112, 1st Paragraph (Enablement) – Claims 1 to 18

The Examiner has further rejected claims 1 to 18 on the grounds that the specification allegedly does not provide enablement for the treatment of inflammation in a mammal associated with a disease characterized by furin or furin-like protease activity using a compound capable of inhibiting a proprotein convertase.

Claims 1 to 18 have been cancelled thus rendering moot the rejection thereto. Applicant respectfully submits that new claims 21 to 40 satisfy the enablement requirement for treating inflammatory/erosive aspects of arthritis using a proprotein protease inhibitor.

Support in the specification for a "proprotein convertase", a "derivative of PDX", and "proprotein convertase inhibitors", are discussed above.

The enablement section of 35 U.S.C. § 112, first paragraph, "requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". *In re Fisher* (427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)).

Further, it is well established under 35 U.S.C. §112 that for a specification to be enabling, it must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation". *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988)); *In re Fisher* (427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)) (the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification). Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. *In re Marzocchi* (439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971)).

The courts have also emphasized that the fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive". In other words, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed". *Ex parte Jackson* (217 USPQ 804, 807 (1982)).

Applicant respectfully submits that the disclosure satisfies the enablement requirement of 35 USC §112, first paragraph since (1) working examples regarding the use of proprotein convertase inhibitors to treat the inflammatory/erosive aspects of arthritis are provided, (2) adequate guidance to practice the invention is provided in the specification, and (3) the extrapolation of *in vitro* data to an *in vivo* method of use using art-accepted cell lines and animal models provides a significant probability that one of skill in the art would successfully obtain the invention as claimed without undue experimentation (see Example 9, pages 28 to 29).

35 USC §112, 2nd Paragraph – Claims 2, 4 and 19

Claims 2, 4 and 19 have been cancelled thus rendering moot the indefiniteness objections thereto.

Objection under 37 CFR §1.75(c) - Claims 2 and 4

Claims 2 and 4 have been cancelled thus rendering moot the objection thereto.

35 USC §102(e) - Claims 1 to 8 and 11 to 16

The Examiner has applied Thomas *et al.* (US 6,022,855) and Jean *et al.* (WO 99/51624) alleging that claims 1 to 8 and 11 to 16 lack novelty in view of one or the other of these references.

Claims 1 to 8 and 11 to 16 have been cancelled thus rendering moot the rejection thereto. Applicant respectfully submits that new claims 21 to 40 are novel and patentably distinguishable over the prior art.

MPEP §2131 provides that:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The **identical invention** must be shown in as complete detail as contained in the ... claim." [Emphasis added.] *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim.

It is respectfully submitted that neither Thomas *et al.* nor Jean *et al.* anticipate the invention, as claimed, because neither reference discloses or teaches a method of treating the inflammatory and/or erosive aspects of arthritis by administering a proprotein convertase inhibitor.

35 USC §103(a) - Claims 1 to 19

Claims 1 to 19 have been rejected as obviousness over Thomas *et al.* (US 6,022,855) and Jean *et al.* (WO 99/51624) in view of Blanchette *et al.*, Schlondorff *et al.*, Wang *et al.*, or Yamanishi *et al.*

Claims 1 to 19 have been cancelled thus rendering moot the rejections thereto. Applicant respectfully submits that new claims 21 to 40 are inventive and patentably distinguishable over the prior art.

In order to establish a *prima facie* case of obviousness, the prior art references(s) must teach or suggest all of the elements and limitations recited in the claims.

Further, in order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned (see MPEP 2141(a) Analogous and Nonanalogous Art).

Thomas et al. disclose inhibitors of furin endoprotease that are variants of α1-antitrypsin, their expression in human cell lines and ability to attenuate or prevent viral and bacterial protein maturation.

Jean et al. disclose methods and reagents for inhibiting furin endoprotease activity to attenuate or prevent viral protein maturation, and thereby alleviate viral infections. Also disclosed are methods for using furin endoprotease inhibition to attenuate or prevent proteolytic processing of bacterial toxins, thereby alleviating bacterial infections. Peptides, peptide analogues, peptide derivatives and peptido-, organo- and chemical mimetics of said peptide inhibitors of furin endoprotease activity as also described, as well as compositions of therapeutically effective amounts of furin endoprotease inhibitors.

Blanchette et al. disclose that TGFβ1 is efficiently processed by furin and that TGFβ1 upmodulates *fur* gene expression in rat synovial cells, which may in turn increase pro-TGFβ1 maturation. Among other things, the results establish that TGFβ1 is efficiently processed by

furin, synovial cells play a major role in rheumatoid arthritis and that cultured rat synovial cells are a good model for the study of furin expression in inflammation.

Schlondorff et al. disclose characterization of TACE maturation (by furin) and localization using human cell lines such as THP-1, COS-7, HeLa, MDA-MB-468 using AEBSF to inhibit the maturation of TACE. AEBSF is a large spectrum serine protease inhibitor.

It is respectfully submitted that none of the above references, taken either individually or in combination, disclose or teach all of the elements/steps of the claimed method of treating the inflammatory and/or erosive aspects of arthritis by administering a proprotein convertase inhibitor. Thomas *et al.* and Jean *et al.* are directed to viral/bacterial infections which is not only completely unrelated to Applicant's field of endeavor, but which are also irrelevant to solving the specific problem with which the Applicant was concerned, i.e. treating the inflammatory/erosive aspects of arthritis. Accordingly, Applicant respectfully submits that the claimed invention is inventive and patentably distinguishable over the prior art.

Wang et al. and Yamanishi et al.

Applicant respectfully submits that neither the Wang *et al.* reference, nor the Yamanishi *et al.* reference are citable under 35 USC §103(a) against the claimed subject matter.

- The Wang *et al.* reference was published on April 9, 2004, which is after June 26, 2000, the priority date of the instant application (based on USSN 60/213,995).

- The Yamanishi *et al.* reference was published in 2002, which is after June 26, 2000, the priority date of the instant application (based on USSN 60/213,995).

Accordingly, Applicant respectfully requests that Wang *et al.* and Yamanishi *et al.* be removed from the record as prior art.

In view of the forgoing, early favorable consideration of this application is earnestly solicited.

It is believed this responds to all of the Examiner's concerns, however if the Examiner has any further questions, she is invited to contact Joy D. Morrow (Reg. No. 30,911) at 613-232-2486. Further, If the Examiner does not consider that the application is in a form for allowance, an interview with the Examiner is respectfully requested.

Respectfully submitted,

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By _____

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